

FIG. 1a.

CYP3A5 Genotype/Phenotype Relationship

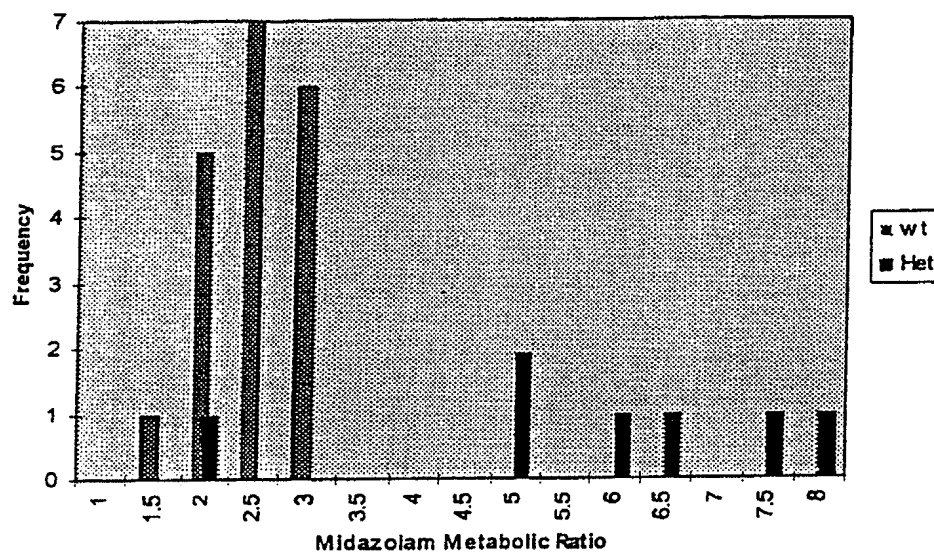


FIG. 1b.

CYP3A5 mRNA Expression Related to Genotype

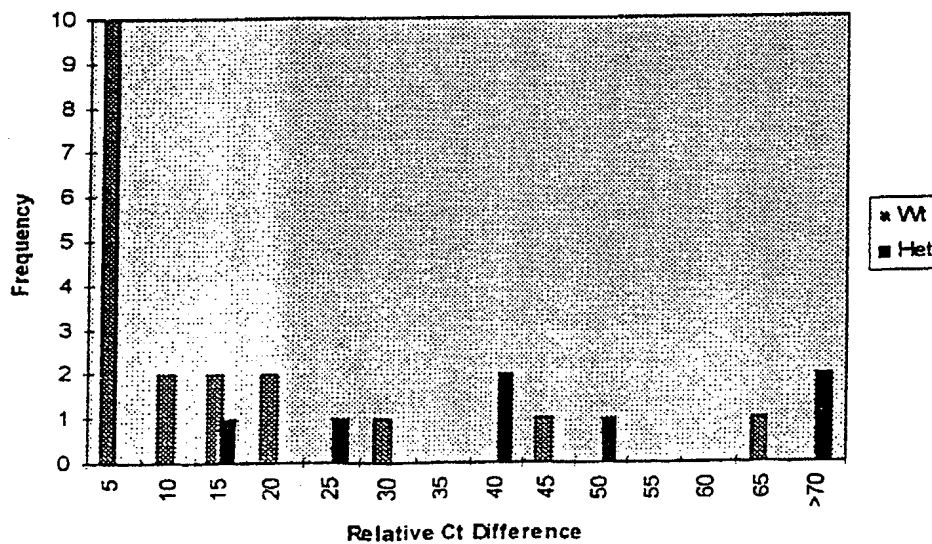
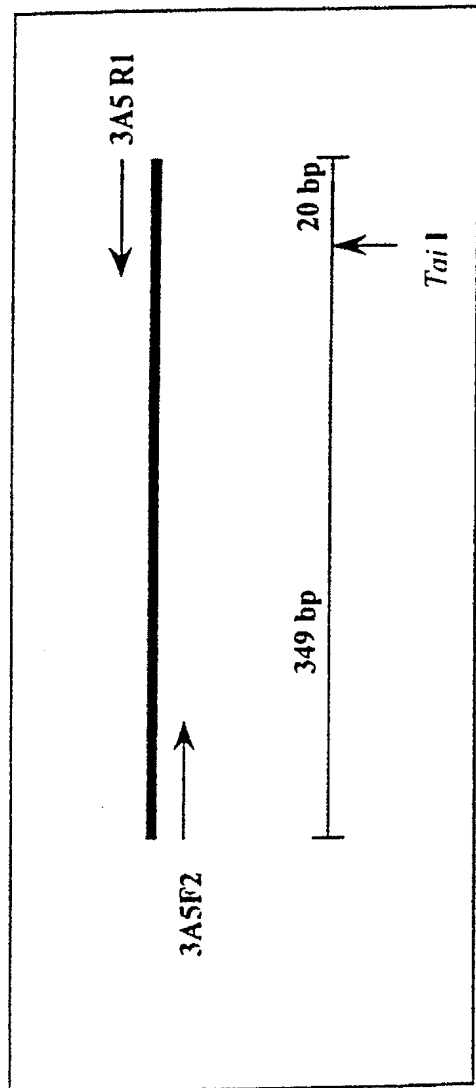
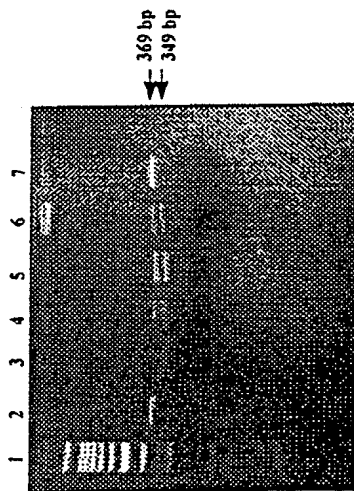


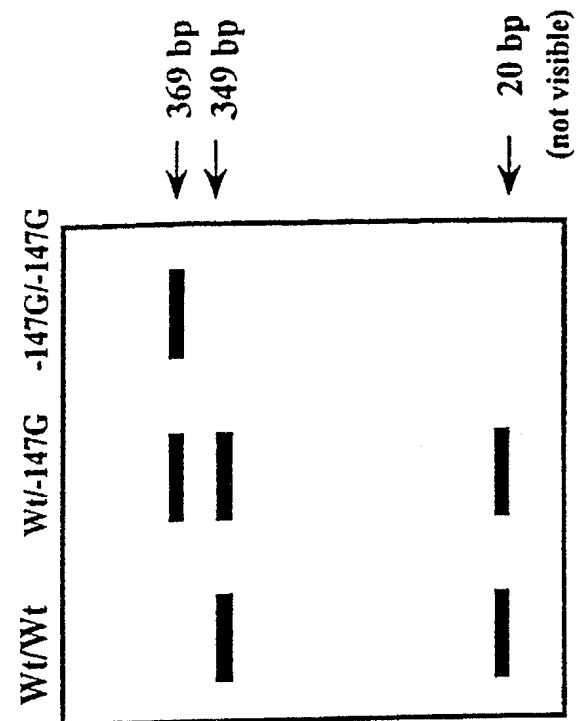
FIG. 2.



2a.



2c.



2b.

FIG. 3.

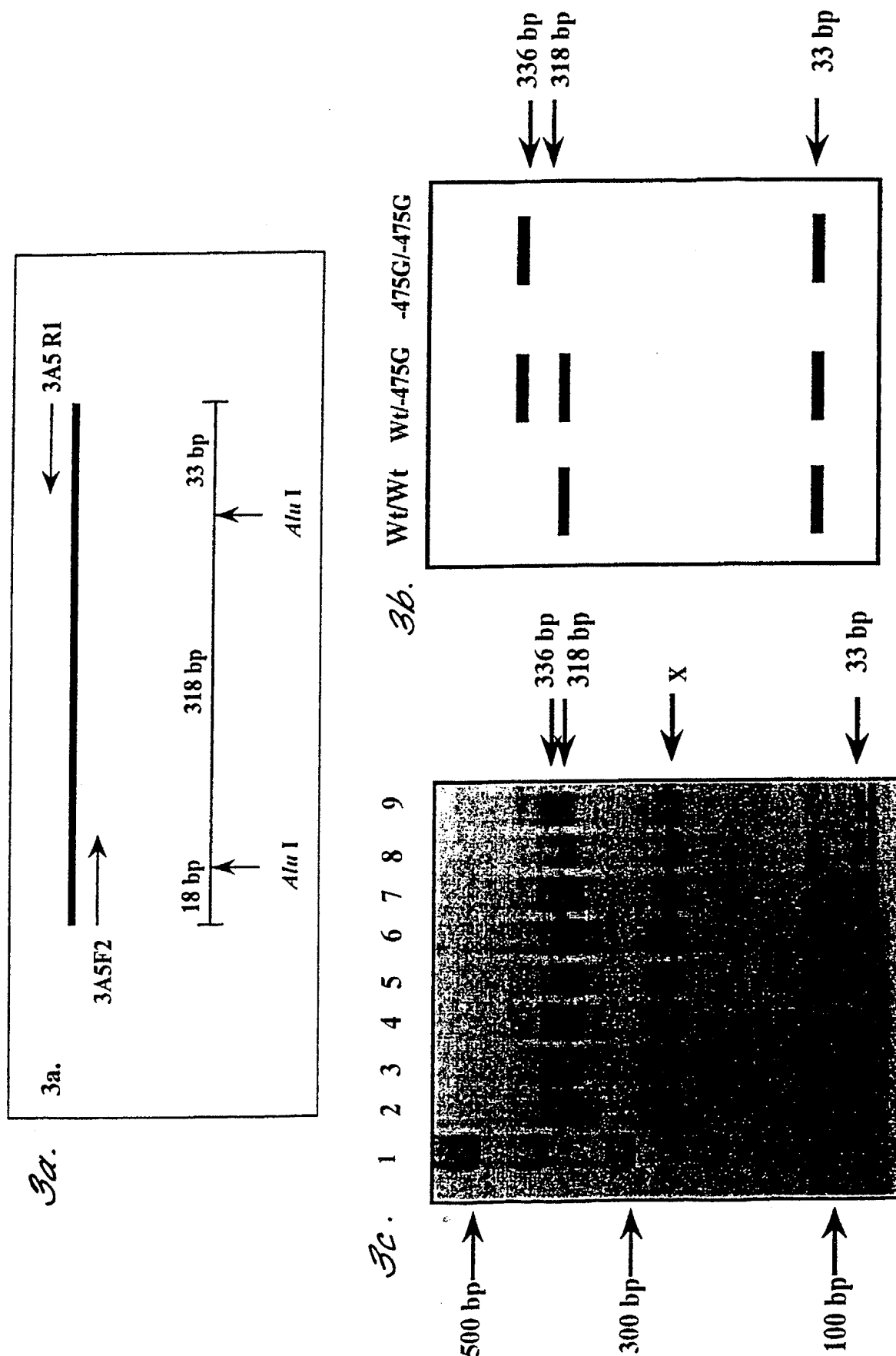


FIG. 4a.

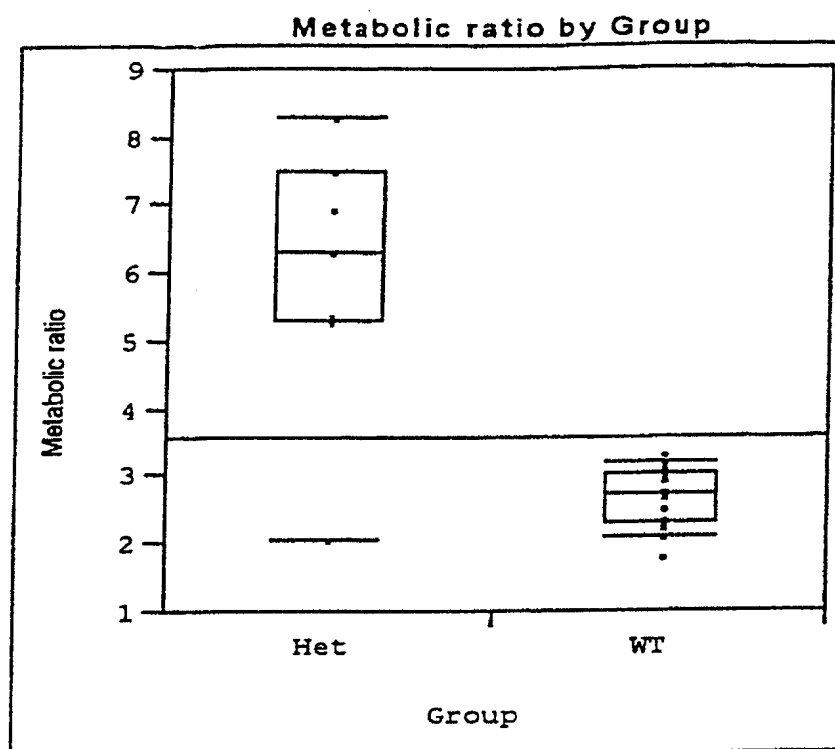
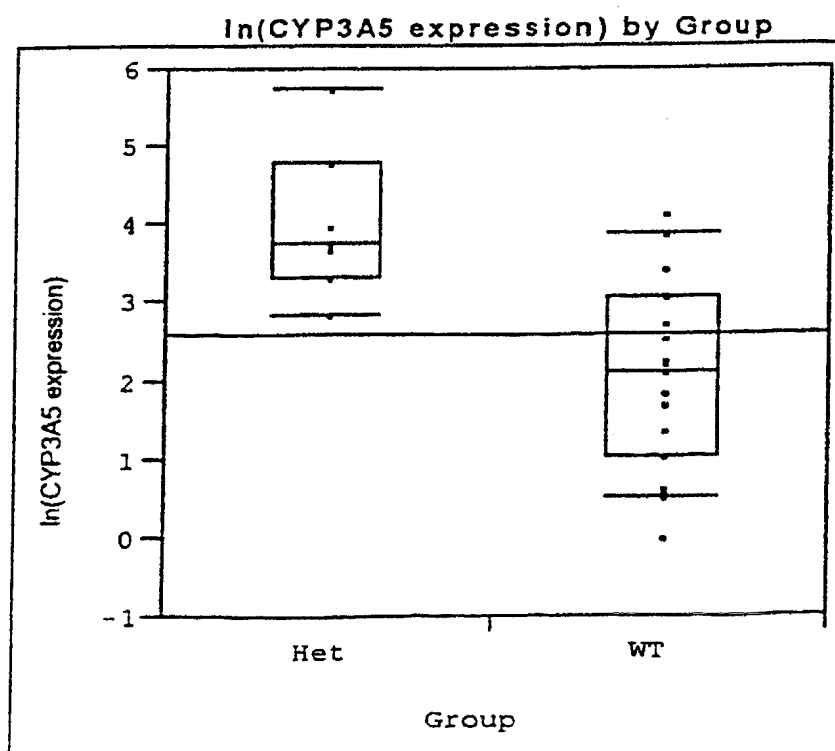


FIG. 4b.



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FIG. 5.

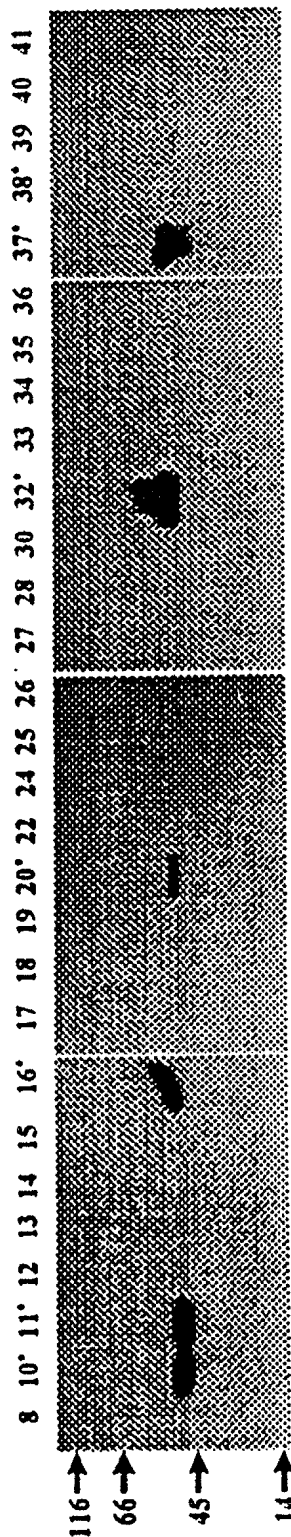


FIG. 6.

3A5F1 5'-GGGTCTGTCTGGCTGCGC-3'

3A5F2 5'-GGGGTCTGTCTGGCTGAGC-3'

3A5R1 5'-TTTATGTGCTGGAGAAGGACG-3'

FIG. 7.

-1343 GGAAGCAACC TACATGTCCA TCAACAGATG AATGGGTAA GAGAGTACTT CACTTATGCA CAATGGAGTA
-1273 CAATTCAGCC ATGAAAAAAG CATGAGATCC TGTCCCTTTAT AATAACGTGG CTGGAACCTGC AGGTCAATTAT
-1203 GTTAGGTAA ATAAGCCAGG CACACAAAGA CAGACATTGC ATGTTCTCAC TTATTGTGG GATCTACAAA
-1133 TCAAAACAAT TGAGCTAATG TCTGGGTCTT AGTCAATTTT GTACCCTAAG TACAGGGAGC ACAGCCATTA
-1063 GAATACATGA TGAATGCTTT AATACAGGAA TGAATAGGTG AGAGGCACAG GGTGGTTGGG TGTCTTCTG
-993 ATACATAGTA TCTTCCTTGA CACATTTCAGT ACAACTCTCA ACAGGTAAGT CTCTTCATGT ATGTTACCTT
-923 CTGAGGAATT AAGTGGCAGA ACATGCCCTC TATTATTTTC CTTTCAGAA CAAGACCAAT TGCATTAGTT
-853 GGGAAACAGT GCTGGCTGCA TCTGAGCCCC AAGCAACCAT TAGTCTATTG CTATCACCAC AGACTCAGAG
-783 GGGATGACAC ACAGGGGCCC AGCAATCTCA CCCAAGTCAA CTCCACCAAC ATTTCTGGTC ACCCACCATG
-713 TGTACAGTAC CCTGCTAGGG TCCAGGGTCA TGAAAGTAA TAATACCAGA CTGTGCCCTT GAGGAACCTCA
-643 CCTCTGCTAA GGGAAACAGG CACAGAAACC CACAAGGGTG GTAGAGAGGA AATAGGACAA TAGGACTGTG
-573 TGAGGGGGAT AGGAGGCACC CAGAGGAGGA AATGGTTACA TCTGTGTGAG GAGGTTGGTA AGGAAAGACT
-503 TTAATAGAAG GGGTCTGTCT GGCTGGGCTT GCAAGGATGT GTAGGAGTCA TCTAGGGGGC ACAAGTACAC
-433 TCCAGGCAGA GGGAATTGCA TGGGTAAAGA TCTGCAGTTG TGGCTTGTGG GGATGGATTT CAAGTATTCT
-363 GGAATGAAGA CAGCCATGGA AACAAAGGCA GGTGAGAGGA TATTTAAGAG GCTTCATGCC AATGGCTCCA
-293 CTTCAGTTTC TGATAAGAAC TCAGGTTCCG TGGACTCCCT GATAAACTG ATTAAGTTGT TTATGATTCC
-223 CCATAGAATA TGAACCTAAA GGAGGTAAGC AAAGGGGTGT GTGCGATTCT TTGCTACTGG CTGCAGCTGC

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FIG. 7 (CONTINUED)

-153 AGCCCCACCT CCTTCTCCAG CACATAACA TTTCAGCAGC TTGACCTAAG ACTGCTGTGC AGGGCAGGGA
 -83 TGCTCCAGGC AGACAGGCCA GCAACAACA GCACACAGCT GAAAGTAAGA CTCAGAGGAG ACAGTTGAAG
 -13 AAGGCAAGTG GCGATG

Variant Sequences in the 5' flanking region of CYP3A5

Position	Variant sequence	Percentage
-1317	G-K (T or G) heterozygote	2.8% (1/36)
-988	T-Y (C or T) heterozygote	8.3% (3/36)
-657	C-Y (C or T) heterozygote	8.3% (3/36)
-475	T-K (T or G) heterozygote	30.6% (11/36)
-264	G-R (G or A) heterozygote	2.8% (1/36)
-147	A-R (A or G) heterozygote	30.6% (11/36)

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FIG. 8.

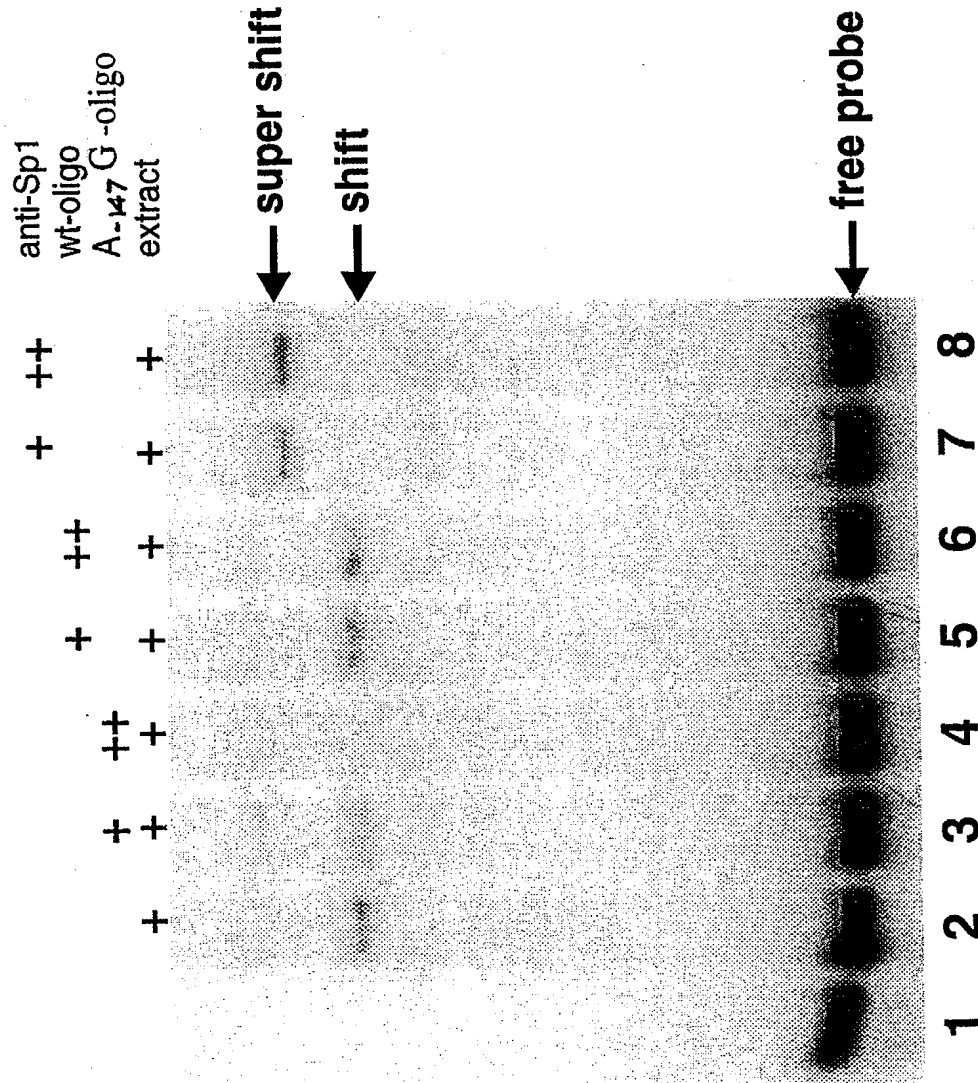


FIG. 9.

CYP3A4, CYP3A5, CYP3A6/7

		*	20	*	40	*	60	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	TA A T	TTGCTGTAGATTATTA	AA A	TATAGCTA	GGTTTGGTGGCTT	T A A A A	60
		*	80	*	100	*	120	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	ATGTAATA	ATTAAATGGA	TAT	ATTAGAT	AGAAAT	GGTG	120
		*	140	*	160	*	180	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	AGGAAG	ATGGAAT	ATATAT	TTCAG	AGATAT	ATG	180
		*	200	*	220	*	240	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
		*	260	*	280	*	300	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
		*	320	*	340	*	360	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
		*	380	*	400	*	420	
sites	:	-----	-----	-----	-----	-----	-----	-
HSCYPFLA_CYP3A6/7	:	-----	-----	-----	-----	-----	-----	-
HSRCYP3_CYP3A7	:	-----	-----	-----	-----	-----	-----	-
HSP4503A4_CYP3A4	:	-----	-----	-----	-----	-----	-----	-
S74699_CYP3A5	:	-----	-----	-----	-----	-----	-----	-
S74700_CYP3A5	:	-----	-----	-----	-----	-----	-----	-

FIG. 9 (CONTINUED 1).

CYP3A4, CYP3A5, CYP3A6/7

		*	440	*	460	*	480		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	GGGAGGGGG	TTTGGG	AAAG	TTCTTAA	TAG	TTT	TGG	168
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	332
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	477
		*	500	*	520	*	540		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	207
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	391
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	537
		*	560	*	580	*	600		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	255
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	450
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	597
		*	620	*	640	*	660		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	303
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	508
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	656
		*	680	*	700	*	720		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	349
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	568
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	716
		*	740	*	760	*	780		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	391
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	628
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	776
		*	800	*	820	*	840		
sites	:	-----		-----		-----			-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-
HSRCYP3_CYP3A7	:	-----		-----		-----			-
HSP4503A4_CYP3A4	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	451
S74699_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	688
S74700_CYP3A5	:	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	TTTGGG	836

FIG. 9 (CONTINUED 2)

CYP3A4, CYP3A5, CYP3A6/7

		*	860	*	880	*	900			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	GTG	AGTA	TGCT	GGGA	AGGC	ATG	GGGA	ATG	511
S74699_CYP3A5	:	GTG	AGTA	TG	TGGGT	AGGGT	ATG	AGTA	ATG	747
S74700_CYP3A5	:	GTG	AGTA	TG	TGG	AGGGT	ATG	AGTA	ATG	893
		*	920	*	940	*	960			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	GGG	ATG	TGCT	GGGA	AGGC	ATG	GGGA	ATG	569
S74699_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	807
S74700_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	950
		*	980	*	1000	*	1020			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	GGG	ATG	TGCT	GGGA	AGGC	ATG	GGGA	ATG	629
S74699_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	867
S74700_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	1010
		*	1040	*	1060	*	1080			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	TGCT	CTG	AGG	CTT	TGGT	GGT	AGG	ATG	688
S74699_CYP3A5	:	TGCT	CTG	AGG	GGT	TGGT	AGG	ATG	ATG	927
S74700_CYP3A5	:	TGCT	CTG	AGG	GGT	TGGT	AGG	ATG	ATG	1068
		*	1100	*	1120	*	1140			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	GGG	ATG	TGCT	GGGA	AGGC	ATG	GGGA	ATG	736
S74699_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	987
S74700_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	1128
		*	1160	*	1180	*	1200			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	GGG	ATG	TGCT	GGGA	AGGC	ATG	GGGA	ATG	796
S74699_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	1046
S74700_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	1187
		*	1220	*	1240	*	1260			
sites	:	-----		-----		-----			-	
HSCYPFLA_CYP3A6/7	:	-----		-----		-----			-	
HSRCYP3_CYP3A7	:	-----		-----		-----			-	
HSP4503A4_CYP3A4	:	GGG	ATG	TGCT	GGGA	AGGC	ATG	GGGA	ATG	856
S74699_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	1105
S74700_CYP3A5	:	GGG	ATG	TG	TGG	AGGC	ATG	GGGA	ATG	1247

FIG. 9(CONTINUED 3).

CYP3A4, CYP3A5, CYP3A6/7

sites :
 HSCYPFLA_CYP3A6/7 :
 HSRYP3_CYP3A7 :
 HSP4503A4_CYP3A4 :
 S74699_CYP3A5 :
 S74700_CYP3A5 :

* 1280 * 1300 * 1320
 916
 1165
 1307

sites :
 HSCYPFLA_CYP3A6/7 :
 HSRYP3_CYP3A7 :
 HSP4503A4_CYP3A4 :
 S74699_CYP3A5 :
 S74700_CYP3A5 :

* 1340 * 1360 * 1380
 976
 1224
 1366

sites :
 HSCYPFLA_CYP3A6/7 :
 HSRYP3_CYP3A7 :
 HSP4503A4_CYP3A4 :
 S74699_CYP3A5 :
 S74700_CYP3A5 :

* 1400 * 1420 * 1440
 55
 1036
 1242
 1383

sites :
 HSCYPFLA_CYP3A6/7 :
 HSRYP3_CYP3A7 :
 HSP4503A4_CYP3A4 :
 S74699_CYP3A5 :
 S74700_CYP3A5 :

* 1460 * 1480 * 1500
 ENHANCER TATA
 62
 115
 1096
 1286
 1427
 gc c ata

sites :
 HSCYPFLA_CYP3A6/7 :
 HSRYP3_CYP3A7 :
 HSP4503A4_CYP3A4 :
 S74699_CYP3A5 :
 S74700_CYP3A5 :

* 1520 * 1540 * 1560
 40
 174
 1156
 1345
 1486
 gg cagg gctcca ca a agcccagcaaa a ca c

sites :
 HSCYPFLA_CYP3A6/7 :
 HSRYP3_CYP3A7 :
 HSP4503A4_CYP3A4 :
 S74699_CYP3A5 :
 S74700_CYP3A5 :

* 1580 * 1600 *
 START-ATG : 70
 94
 228
 1210
 1399
 1540
 ac gctgaaa aagactcagaggaga ag t a aagg aagT G gATG

FIG. 9(a).

```

      A or G
      =
MEME repeated motif 9
=====
      MEME 'single' motif 9
=====
      Yi-consensus
      =====
      apoE-undefined-site-3
      =====
      ApoE_B1
      =====
      APRT-human_US
      =====
      APRT-CHO_US
      =====
1238 AGCTGCAGCCCCABCCCTCCTTCTCCAGC
      TCGACGTCGGGGTGGAGGAAGAGGTCG
      .....

```

FIG. 9(b).

```

MEME repeated motif 2
=====
MEME repeated motif 2
=====
      MEME 'single' motif 9
=====
      Yi-consensus
      =====
      Sp1-TPI_(4)
      =====
      GCF-consensus
      =====
      DSE_(1)
      =====
      IRE_(1)
      =====
      Sp1_CS4
      =====
      GC-box_(1)
      =====
      Sp1-IE-4/5
      =====
      Sp1-IE-3.3
      =====
      E2A_CS hsp70.2
      =====
      E2A_CSSp1-hsp70_(1)
      =====
      APRT-mouse_US
      =====
1379 AGCTGCAGCCCCGBCCTCCTTCTCCAGC
      TCGACGTCGGGGCGGAGGAAGAGGTCG
      .....

```

FIG. 9(c).

```

MEME repeated motif 9
=====
MEME repeated motif 9
=====
MEME repeated motif 3
=====
MEME 'single' motif 6
=====
E-2.7_kb_(3)
=
E1A-F_CS
=====
MTVGRE_NRS
=====
GH1
=====
910 TCTGTCTGGCTGGGCTTGCAAGGATGTGTAG
AGACAGACCGACCCGAACGTTCTACACATC

```

(A)_T*FIG. 9(d).*

```

MEME repeated motif 9
=====
MEME repeated motif 9
=====
MEME repeated motif 9
=====
MEME repeated motif 3
=====
MEME 'single' motif 6
=====
E-2.7_kb_(3)
=
MBF-I_CS
=====
E1A-F_CS
=====
CNBP-SREMTVGRE_NRS
=====
GH1 MRE_CS2
=====
1052 TCTGTCTGGCTGGCGTGCAAGGATGTGTAG
AGACAGACCGACCGCACGTTCTACACATC

```

(A)_G